

62. A method for detecting intracellular integrase activity using a promoterless reporter gene.
63. The method according to claim 62, wherein integrase activity is present after transfection of an integrase gene.
64. The method according to claim 62 wherein integrase activity is performed by means of a wild type or mutated integrase protein.
65. The method according to claim 62, wherein integrase activity is performed by means of a retroviral integrase protein.
66. The method according to claim 62, wherein integrase activity is performed by means of an HIV integrase.
67. The method according to claim 62, wherein the reporter gene is one of a luciferase, GFP, an antibiotic selection marker and a cytotoxic drug resistance gene.
68. A method for detecting intracellular integrase activity using a promoterless reporter gene, wherein a reporter gene construct is generated from the reporter gene and the construct is used as the substrate of an enzymatically active retroviral protein expressed from a synthetic retroviral pol or gag gene, the synthetic gene having modified codon usage compared with a wildtype gene, the synthetic gene being for expression of a retroviral pol or gag gene or a region of a retroviral pol or gag gene in a eukaryotic cell, and the expressed retroviral protein being at a level to provide detectable activity of a wild type

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function of the expressed retroviral protein in the eukaryotic cell.

69. The method according to claim 68, wherein the gene or region thereof, after codon optimisation for a eukaryotic host for which it is expressed, contains a GC nucleotide pair content between 53 and 63% and the expressed gene is expressed at a level to provide detectable enzymatic activity of the expressed retroviral protein in the eukaryotic cell.
70. The method according to claim 68, wherein the retroviral protein is an HIV gag or pol protein or a fragment thereof.
71. The method according to claim 68, wherein the detectable enzymatic activity includes at least promotion or stimulation of the integration of DNA fragments into the host cell DNA.
72. The method according to claim 68, wherein the expressed protein has an expression level of at least 200 % compared to the expressed wild type gene in a eukaryotic cell.
73. The method according to claim 68, wherein the reporter gene construct contains an internal IRES.
74. An integrase inhibitor obtained by screening for the inhibitor using the method of claim 62.
75. A packaging construct for a lentiviral or complex retroviral vector based on a synthetic retroviral pol or gag gene, the synthetic gene having modified codon usage compared with a

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wildtype gene, the synthetic gene being for expression of a retroviral pol or gag gene or a region of a retroviral pol or gag gene in a eukaryotic cell, the expressed retroviral protein being at a level to provide detectable activity of a wild type function of the expressed retroviral protein in the eukaryotic cell.

76. A packaging construct according to claim 75, wherein the gene or region thereof, after codon optimisation for a eukaryotic host in which it is expressed, contains a GC nucleotide pair content between 53 and 63 %, and the expressed gene is expressed at a level to provide detectable enzymatic activity of the expressed retroviral protein in the eukaryotic cell.
77. A packaging construct according to claim 76, wherein the retroviral protein is an HIV gag or pol protein or a fragment thereof.
78. A packaging construct according to claim 76, wherein the detectable activity of the enzymatic function includes at least promotion or stimulation of the integration of DNA fragments into the host cell DNA.
79. A packaging construct according to claim 76, wherein the retroviral protein is a protease, a reverse transcriptase, an integrase or a polyprotein gag-pol precursor thereof.

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80. A packaging construct according to claim 76, wherein the expressed protein has an expression level of at least 200 % compared to the expressed wild type gene in a eukaryotic cell.

81. A method for preparing a synthetic gene or part of a gene encoding a retroviral protein or part of such a protein which is enzymatically active in a target eukaryotic cell comprising the steps of:

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- (i) identifying a group of genes from the total set of genes of the target eukaryotic cell which encode proteins which are naturally expressed easily and/or in high concentrations in the target cell,
  - (ii) determining the codon sequences of the genes identified in step (i) and, from these codon sequences, a preferred codon usage and a preferred nucleotide pair frequency,
  - (iii) using the preferred codon usage, identify the non-preferred codons in the natural gene encoding the enzymatically active protein, and
  - (iv) replacing one or more of the non-preferred codons with one or more preferred codons encoding the same amino-acids as the replaced codons while biasing the replacement to obtain the preferred nucleotide pair frequency, the preferred nucleotide pair frequency being a GC nucleotide pair content between 53 and 63 %.

82. The method according to claim 81, wherein the replacement step (iv) is carried out on a random choice between alternative codons encoding the same amino-acid at each position using a random number generator and biasing the choice of alternative codons based on the preferred codons on the preferred codon usage to obtain the preferred nucleotide frequency.
83. A synthetic retroviral gag or pol gene or a region of a retroviral gag or pol gene for the expression of a retroviral gag or pol protein in a eukaryotic cell, the retroviral gene having non-preferred codons when referred to the eukaryotic cell, the number of non-preferred codons being such that replacement of all the non-preferred codons by preferred codons for the eukaryotic cell results in a GC dinucleotide pair content of 65 % or higher, the synthetic gene having a nucleotide pair content between 53 and 63 %, and the expressed retroviral protein being expressed at a level to provide detectable enzymatic activity of the expressed retroviral protein in the eukaryotic cell.
84. The synthetic gene according to claim 83, wherein the retroviral protein is an HIV gag or pol protein.
85. The synthetic gene according to claim 83, wherein the detectable enzymatic activity includes at least promotion or stimulation of integration of DNA fragments into the host cell DNA.

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86. The synthetic gene according to claim 83, wherein the retroviral protein is a protease, a reverse transcriptase, an integrase protein or a polyprotein gag-pol precursor thereof.
  87. The synthetic gene according to claim 83, wherein the expression of the protein is at a level of at least 200% of that expressed by the wild type gene in the eukaryotic cell.
  88. A eukaryotic expression vector comprising a synthetic retroviral gag or pol gene or a region thereof in accordance with claim 83.
  89. A method of transfecting a eukaryotic cell by using a eukaryotic expression vector comprising a synthetic retroviral gag or pol gene or a region thereof in accordance with claim 83.
  90. A eukaryotic cell line or a transgenic animal harbouring the synthetic retroviral gag or pol gene or region thereof in accordance with claim 83.
  91. A method for gene transfer into a eukaryotic cell expressing a synthetic retroviral gag or pol gene or region thereof in accordance with claim 83.
  92. A method for gene transfer into a eukaryotic cell expressing a synthetic retroviral gag or pol gene or region thereof in accordance with claim 83, wherein the synthetic gene is transiently expressed or is stably integrated in said cell.
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